### WE CLAIM:

# 1. An isochroman compound having the structure

$$Ar_1$$
  $Ar_2$   $HAr$   $R_9$ 

### wherein

# a) Ar<sub>1</sub> has the structure

$$R_1$$
 $R_2$ 
 $R_3$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_4$ 
 $R_5$ 

wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are independently selected from hydrogen, halogen, amino, and/or substituents comprising 1 to 4 carbon atoms selected from alkyl, haloalkyl, cyano, mono-substituted amino, disubstituted amino, alkoxy, haloalkoxy, carboalkoxy, acyl, alkylcarboxamido, dialkylcarboxamido, alkylamido, acyloxy; and R<sub>5</sub> is selected from hydrogen, a halogen, amino, -SH, or a radical comprising 1 to 4 carbon atoms selected from alkyl, mono-substituted amino, disubstituted amino, alkoxy, haloalkoxy, thioalkyl, or thioacyl;

# b) Ar<sub>2</sub> has the structure

wherein X is an integer selected from 0, 1, or 2, and R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently selected from hydrogen, halogen, amino, nitro, and/or substituents comprising 1 to 4 carbon atoms selected from alkyl, haloalkyl, cyano, mono-substituted amino, di-substituted amino, alkoxy,

haloalkoxy, carboalkoxy, alkylcarboxamido, dialkylcarboxamido, alkylamido, acyloxy, -SH, thioalkyl, or thioacyl;

- c) R<sub>9</sub> is hydrogen, hydroxy, or an alkyl radical comprising 1 to 4 carbon atoms;
- d) ---- is either present or absent; and
- e) HAr has the structure

or a pharmaceutically acceptable salt thereof.

- 2. The compound of claim 1 wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are independently selected from hydrogen and alkyls comprising 1 to 4 carbon atoms; and R<sub>5</sub> is selected from hydrogen, fluorine, amino, -SH, methyl, ethyl, mono-methyl amino, dimethyl amino, methoxy, trifluoromethoxy, or thiomethyl.
- 3. The compound of claim 1 wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are methyl; and R<sub>5</sub> is selected from hydrogen, fluorine, amino, -SH, methyl, ethyl, mono-methyl amino, dimethyl amino, methoxy, trifluoromethoxy, or thiomethyl.
- 4. The compound of claim 1 wherein Ar<sub>2</sub> has the structure

$$R_6$$
  $R_7$   $R_6$   $R_7$   $R_7$   $R_7$   $R_8$   $R_9$   $R_9$ 

5. The compound of claim 1 wherein Ar<sub>2</sub> has the structure

wherein R<sub>6</sub> is halo, methyl, ethyl, isopropyl, hydroxymethyl, hydroxyethyl, amino, methylamino, dimethylamino, hydroxyl, methoxy, or trifluoromethoxy.

6. The compound of claim 1 wherein Ar<sub>2</sub> has the structure

7. The compound of claim 1 wherein  $Ar_2$  has the structure

wherein  $R_6$  is halo, methyl, ethyl, isopropyl, hydroxymethyl, hydroxyethyl, amino, methylamino, dimethylamino, hydroxyl, methoxy, or trifluoromethoxy.

- 8. The compound of claim 1 wherein  $R_9$  is hydrogen.
- 9. The compound of claim 1 wherein ---- is present.
- 10. The compound of claim 1 wherein HAr has the structure

11. The compound of claim 1 having the formula

5-[2,5-Difluoro-4-methoxy-3-(1,1,4,4,7-pentamethyl-isochroman-6-yl)-benzylidene]-thiazolidine-2,4-dione;

5-[3-(1,1,4,4,7-Pentamethyl-isochroman-6-yl)-4-trifluoromethoxy-benzylidene]-thiazolidine-2,4-dione;

5-[4-Dimethylamino-3-(1,1,4,4,7-pentamethyl-isochroman-6-yl)-benzylidene]-thiazolidine-2,4-dione;

5-[3-(7-Chloro-1,1,4,4-tetramethyl-isochroman-6-yl)-4-trifluoromethoxybenzylidene]-thiazolidine-2,4-dione

5-[2,5-Difluoro-4-methoxy-3-(1,1,4,4,7-pentamethyl-isochroman-6-yl)-benzylidene]-thiazolidine-2,4-dione;

5-[3-(1,1,4,4,7-Pentamethyl-isochroman-6-yl)-4-trifluoromethoxy-benzylidene]-thiazolidine-2,4-dione;

5-[4-Dimethylamino-3-(1,1,4,4,7-pentamethyl-isochroman-6-yl)-benzylidene]-thiazolidine-2,4-dione; and

- 5-[3-(7-Chloro-1,1,4,4-tetramethyl-isochroman-6-yl)-4-trifluoromethoxybenzylidene]-thiazolidine-2,4-dione.
- 12. A pharmaceutical composition comprising one or more of the compounds of claim 1 or pharmaceutically acceptable salts or prodrugs thereof, and one or more pharmaceutically acceptable carriers.
- 13. A method for the treatment of a disease of uncontrolled cellular proliferation comprising administering to a mammal diagnosed as having a disease of uncontrolled cellular proliferation one or more compounds of claim 1 or pharmaceutically acceptable salts or prodrugs thereof, or a pharmaceutical composition thereof, in an amount effective to treat the disease of uncontrolled cellular proliferation.
- 14. The method of claim 13 wherein the disease of uncontrolled proliferation is a carcinoma, lymphoma, leukemia, or sarcoma.
- 15. The method of claim 13 wherein the disease of uncontrolled proliferation is a cancer.
- 16. The method of claim 15 wherein the cancer is lymphoma, Hodgkin's Disease, myeloid leukemia, bladder cancer, brain cancer, head and neck cancer, kidney cancer, lung cancers such as small cell lung cancer and non-small cell lung cancer, myeloma, neuroblastoma/glioblastoma, ovarian cancer, pancreatic cancer, prostate cancer, skin cancer, liver cancer, melanoma, colon cancer, cervical carcinoma, breast cancer, or epithelial cancer.
- 17. The method of claim 15 that additionally comprises administration of one or more additional therapeutic agents effective for the treatment of the cancer.
- 18. A method of modulating lipid metabolism, carbohydrate metabolism, or lipid and carbohydrate metabolism comprising administering to a mammal diagnosed as needing such modulation one or more of the compounds of claim 1 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to induce such modulation.
- 19. A method of treating hypercholesterolimia comprising administering to a mammal diagnosed as needing such treatment one or more compounds of claim 1 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to treat the hypercholesterolimia.

- 20. The method of claim 19, wherein the one or more compounds is applied in an amount effective to decrease serum cholesterol levels by at least about 5%.
- 21. A method of treating dyslipidemia comprising administering to a mammal diagnosed as needing such treatment one or more compounds of claim 1 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to decrease serum triglyceride levels.
- 22. The method of claim 21, wherein the one or more compounds are applied in an amount effective to decrease serum triglyceride levels by at least about 5%.
- 23. A method of treating Type 2 Diabetes comprising administering to a mammal diagnosed as needing such treatment one or more compounds of claim 1 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to treat the Type 2 Diabetes.
- 24. The method of claim 23, wherein the compound is applied in an amount effective to to decrease the serum glucose levels in the mammal by at least about 5%.
- 25. The method of claim 24 wherein the administration is also effective to decrease serum triglyceride levels in the mammal by at least about 5%.
- 26. The method of claim 23 wherein the mammal is a human.
- 27. A dihydronaphthalene compound having the structure

$$Ar_1$$
  $Ar_2$   $HAr$   $R_9$ 

wherein

a)  $Ar_1$  has the structure

wherein  $R_0$  is selected from hydrogen, a halogen, an aryl or heteroaryl comprising 1 to 8 carbon atoms, and radicals comprising 1 to 4 carbon atoms selected from alkyl, haloalkyl, di-substituted amino, alkoxy, haloalkoxy, or acyloxy; and  $R_{10}$ ,  $R_{20}$ ,  $R_{30}$ , and  $R_{40}$  are independently selected from substituents comprising 1 to 4 carbon atoms selected from

alkyl, haloalkyl, cyano, amino, mono-substituted amino, di-substituted amino, alkoxy, haloalkoxy, carboalkoxy, alkylcarboxamido, dialkylcarboxamido, alkylamido, or acyloxy, and R<sub>50</sub> is selected from hydrogen, a halogen, amino, -SH, or a radical comprising 1 to 4 carbon atoms selected from alkyl, mono-substituted amino, di-substituted amino, alkoxy, haloalkoxy, thioalkyl, or thioacyl;

b) Ar<sub>2</sub> has the structure

wherein X is an integer selected from 0, 1, or 2, and  $R_6$ ,  $R_7$  and  $R_8$  are independently selected from hydrogen, halogen, amino, nitro, and substituents comprising 1 to 4 carbon atoms selected from alkyl, haloalkyl, cyano, mono-substituted amino, di-substituted amino, alkoxy, haloalkoxy, carboalkoxy, alkylcarboxamido, dialkylcarboxamido, alkylamido, acyloxy, -SH, thioalkyl, or thioacyl;

- c) R<sub>9</sub> is hydrogen, hydroxy, or an alkyl radical comprising 1 to 4 carbon atoms;
- d) ---- is either present or absent; and
- e) HAr has the structure

or a pharmaceutically acceptable salt thereof.

28. The compound of claim 27 wherein R<sub>10</sub>, R<sub>20</sub>, R<sub>30</sub>, and R<sub>40</sub> are independently selected from hydrogen, and alkyls comprising 1 to 4 carbon atoms; and R<sub>0</sub> is hydrogen, fluorine, phenyl, fluorophenyl, benzyl, hydroxyphenyl, pyridyl,

methyl, ethyl, propyl, isopropyl, trifluoromethyl, dimethyl amino, methoxy, or trifluoromethoxy.

- 29. The compound of claim 27 wherein R<sub>10</sub>, R<sub>20</sub>, R<sub>30</sub>, and R<sub>40</sub> are methyl; and R<sub>50</sub> is selected from hydrogen, fluorine, amino, -SH, methyl, ethyl, mono-methyl amino, dimethyl amino, methoxy, trifluoromethoxy, and thiomethyl, and R<sub>0</sub> is hydrogen, fluorine, phenyl, fluorophenyl, benzyl, hydroxyphenyl, pyridyl, methyl, ethyl, propyl, isopropyl, trifluoromethyl, dimethyl amino, methoxy, or trifluoromethoxy.
- 30. The compound of claim 27 wherein Ar<sub>2</sub> has the structure

31. The compound of claim 27 wherein Ar<sub>2</sub> has the structure

$$R_6$$
 or  $R_6$   $R_7$ 

wherein R<sub>6</sub> is halo, methyl, ethyl, isopropyl, hydroxymethyl, hydroxyethyl, amino, methylamino, dimethylamino, hydroxyl, methoxy, or trifluoromethoxy.

32. The compound of claim 27 wherein Ar<sub>2</sub> has the structure

33. The compound of claim 27 wherein Ar<sub>2</sub> has the structure

wherein R<sub>6</sub> is halo, methyl, ethyl, isopropyl, hydroxymethyl, hydroxyethyl, amino, methylamino, dimethylamino, hydroxyl, methoxy, or trifluoromethoxy.

- 34. The compound of claim 27 wherein R<sub>9</sub> is hydrogen.
- 35. The compound of claim 27 wherein ---- is present.

### 36. The compound of claim 27 wherein HAr has the structure

- 37. The compound of claim 27 having the formula
  - 5-[4-Dimethylamino-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[2,5-Difluoro-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-4-methoxybenzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Trifluoromethoxy-3-(3,5,5-trimethyl-8-phenyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Trifluoromethoxy-3-(3,5,5-trimethyl-8-thiophen-2-yl-5,6-dihydronaphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Trifluoromethoxy-3-(3,5,5-trimethyl-8-thiophen-3-yl-5,6-dihydronaphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Trifluoromethoxy-3-(3,5,5-trimethyl-8-thiophen-2-yl-5,6-dihydronaphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[2,5-Difluoro-4-methoxy-3-(3,5,5,8,8-pentamethyl-5,8-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[3-(3,5,5,8,8-Pentamethyl-5,8-dihydro-naphthalen-2-yl)-4-trifluoromethoxy-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Dimethylamino-3-(3,5,5,8,8-pentamethyl-5,8-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Ethoxy-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]- thiazolidine-2,4-dione;
  - 5-[4-Ethylamino-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Ethyl-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
  - 5-[4-Chloro-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;

- 5-[3-Bromo-5-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
- 5-[4-(Ethyl-methyl-amino)-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydronaphthalen-2-yl)-benzylidene]-thiazolidine-2,4-dione;
- 5-[4-Ethoxy-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-2-thioxo-thiazolidin-4-one;
- 5-[4-Dimethylamino-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-2-thioxo-thiazolidin-4-one; or
- 5-[4-Ethylamino-3-(8-isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-benzylidene]-2-thioxo-thiazolidin-4-one.
- 38. The compound of claim 27 having the formula 5[3-(8-Isopropyl-3,5,5-trimethyl-5,6-dihydro-naphthalen-2-yl)-4-trifluoromethoxy-benzylidene]- thiazolidine-2,4-dione.
- 39. A pharmaceutical composition comprising one or more of the compounds of claim 27 or pharmaceutically acceptable salts or prodrugs thereof, and one or more pharmaceutically acceptable carriers.
- 40. A method for the treatment of a disease of uncontrolled cellular proliferation comprising administering to a mammal diagnosed as having a disease of uncontrolled cellular proliferation one or more compounds of claim 27 or pharmaceutically acceptable salts or prodrugs thereof, or a pharmaceutical composition thereof, in an amount effective to treat the disease of uncontrolled cellular proliferation.
- 41. The method of claim 40 wherein the disease of uncontrolled proliferation is a carcinoma, lymphoma, leukemia, or sarcoma.
- 42. The method of claim 40 wherein the disease of uncontrolled proliferation is a cancer.
- 43. The method of claim 42 wherein the cancer is lymphoma, Hodgkin's Disease, myeloid leukemia, bladder cancer, brain cancer, head and neck cancer, kidney cancer, lung cancers such as small cell lung cancer and non-small cell lung cancer, myeloma, neuroblastoma/glioblastoma, ovarian cancer, pancreatic cancer, prostate cancer, skin cancer, liver cancer, melanoma, colon cancer, cervical carcinoma, breast cancer, or epithelial cancer.

- 44. The method of claim 43 that additionally comprises administration of one or more additional therapeutic agents effective for the treatment of the cancer.
- 45. A method of modulating lipid metabolism, carbohydrate metabolism, or lipid and carbohydrate metabolism comprising administering to a mammal diagnosed as needing such modulation one or more of the compounds of claim 27 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to induce such modulation.
- 46. A method of treating hypercholesterolimia comprising administering to a mammal diagnosed as needing such treatment one or more compounds of claim 27 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to treat the hypercholesterolimia.
- 47. The method of claim 46, wherein the one or more compounds is applied in an amount effective to decrease serum cholesterol levels by at least about 5%.
- 48. A method of treating dyslipidemia comprising administering to a mammal diagnosed as needing such treatment one or more compounds of claim 27 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to decrease serum triglyceride levels.
- 49. The method of claim 48, wherein the one or more compounds are applied in an amount effective to decrease serum triglyceride levels by at least about 5%.
- 50. A method of treating Type 2 Diabetes comprising administering to a mammal diagnosed as needing such treatment one or more compounds of claim 27 or pharmaceutically acceptable salts or prodrugs thereof, in an amount effective to treat the Type 2 Diabetes.
- 51. The method of claim 50, wherein the compound is applied in an amount effective to to decrease the serum glucose levels in the mammal by at least about 5%.
- 52. The method of claim 50 wherein the administration is also effective to decrease serum triglyceride levels in the mammal by at least about 5%.
- 53. The method of claim 50 wherein the mammal is a human.